

Remarks:

Claim amendments

Claim 48 has been amended by importing limitations from claim 34, which has been cancelled. Additional matter incorporated into claim 48 is found on p. 8, third paragraph of the specification. No new matter is added to the claim by the amendment. Accordingly, entry of the amendment is respectfully requested.

Claim 26 is rendered redundant by the amendments to claim 48 on which it depends.

With the entry of the instant amendment, claims 27-32 and 35, 36, 39 and 48 are pending in the application. Claim 48 is the only independent claim.

Claim Rejections under 35 U.S.C. §103

All pending claims were rejected under 35 U.S.C. §103 as obvious over Wittwer et al., U.S. Patent No. 6,174,670 in view of Zimmermann et al., U.S. Patent Application Publication No. 2002/0102548, cited in the previous office action. The rejection is obviated by amendments.

With respect to claim 48, and specifically with respect to hybrids formed by the test and control nucleic acids, the office action stated that Wittwer teaches hybrids that “have melting points sufficiently different to analytically differentiate [them]...when detection is carried out at a temperature that is 2°C to 10°C below the melting point of said detection probe.” However, the new claim limitation reads “having melting points sufficiently different to analytically differentiate said hybrids during said qualitative detection, wherein said control nucleic acid and said probe essentially do not hybridize during said quantitative detection which is carried out at a temperature that is 2 °C to 10 °C below the melting point of said detection probe and said target nucleic acid.”

Wittwer does not teach or suggest a method where BOTH limitations are met: first, “having melting points sufficiently different to analytically differentiate said hybrids during said *qualitative* detection” and second, “said control nucleic acid and said probe essentially do not hybridize during said *quantitative* detection”¹.

¹ The terms “quantitative” and “qualitative” detection are defined on page 7 (last paragraph) of the specification. Quantitative detection is defined as the one taking place during the amplification cycles, while qualitative detection is defined as the post-amplification melt. The examples cited in the office action all involve the post-amplification melt, i.e. the qualitative detection.

Wittwer teaches *qualitative* detection (melt) where several nucleic acid targets “have sufficiently different melting points” to be distinguished. This includes the examples cited by the examiner and shown on Figures 47 and 48. However, there are no examples of *quantitative* detection (amplification curves) where one of the targets “essentially [does] not hybridize” and is not detected. Therefore Wittwer does not teach a method that includes all the limitations of the Applicants’ claim.

MPEP states that even without express teaching, the invention may be *inherent* from the prior art (see MPEP 2112). However, for this to be true “the extrinsic evidence must make clear that the missing descriptive matter *is necessarily present* in the thing described in the reference.” (MPEP 2112(IV)). The intentionally undetectable target is not present in Wittwer’s method. It is contrary to the purposes of Wittwer that one of the nucleic acids is amplified “silently.” For example, in col. 5-7, where amplification and amplification curves are discussed generally, *all targets* are designed to be detected by the probes, without exception. In col. 13-14, Wittwer teaches specifically to include a control which is to be detected together with the test nucleic acid during amplification. Finally, in Example 19, Wittwer expressly requires that one *detect and quantify* the control during amplification as such data has clinical utility. Clearly, the Applicants’ strategy of omitting one of the amplified sequences from detection is antithetical to the goals of Wittwer. Therefore the Applicants’ method is not inherent from the Wittwer reference.

Based on the foregoing, Wittwer is entirely lacking at least one express limitation of the Applicants’ claim 48 and its dependent claims. Zimmermann teaches various control nucleic acids that are detected by a method different from detection methods of Wittwer. Therefore Zimmermann does not fill the gap with respect to the detection method of Wittwer. A hypothetical combination of the two references would fall short of the present invention. For this reason, an obviousness rejection over Wittwer in view of Zimmermann may not be maintained. Withdrawal of the obviousness rejection of claim 48, and its dependent claims is respectfully requested.

Conclusion:

In view of the above, applicants believe that all claims now pending in this application are in condition for allowance. It is believed that no fees are due at this time. However, the Commissioner is authorized to charge any additional fee deficiency, or credit any overpayment, to Deposit Account No. 50-0812.

If the Examiner believes that a telephone conference would expedite prosecution of this application, the examiner is invited to call the undersigned directly at the number below.

Respectfully submitted,

Date: February 13, 2009



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